Asymmetric Intramolecular Alkylation of Chiral Aromatic Imines via Catalytic C–H Bond Activation

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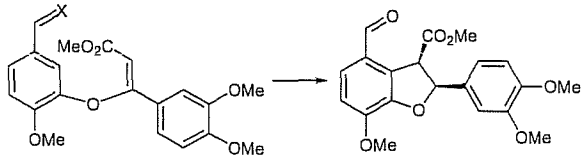
Abstract: The asymmetric intramolecular alkylation of chiral aromatic aldimines, in which differentially substituted alkenes are tethered *meta* to the imine, was investigated. High enantioselectivities were obtained for imines prepared from aminoindane derivatives, which function as directing groups for the rhodium-catalyzed C–H bond activation. Initial demonstration of catalytic asymmetric intramolecular alkylation also was achieved by employing a sterically hindered achiral imine substrate and catalytic amounts of a chiral amine.

Key words: C–H bond activation, asymmetric catalysis, transimination, cyclization, dihydrobenzofuran

The intramolecular alkylation of aromatic imines via rhodium-catalyzed *ortho*-directed C–H bond activation[1] provides an efficient route to functionalized bicyclic ring systems.[2] A catalytic and highly enantioselective variant of this intramolecular alkylation has been achieved for some alkene substitution patterns using chiral phosphoramidite ligands.[3] However, for other alkene substitution patterns, alternative approaches for achieving asymmetric induction may be necessary. In the context of the first total synthesis of (+)-lithospermic acid,[4,5] the first example of employing a chiral imine as a directing group in catalytic C–H bond activation was developed. Specifically, imine **2**, prepared by condensation of **1** with *R*-(–)-aminoindane, was cyclized to give product **3** in 76% ee after auxiliary hydrolysis (Scheme 1). Herein, improved chiral imine directing groups are reported and evaluated with substrates containing different alkene substitution patterns.[4]

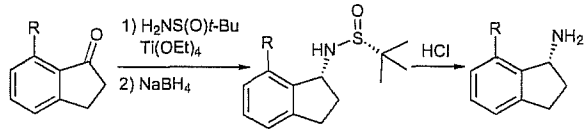


1 X = O
2 X = (*R*)-(–)-aminoindanyl

3

Scheme 1 Asymmetric cyclization of lithospermic acid precursor

In previously published work, we evaluated a range of structurally diverse chiral amine directing groups, with aminoindane proving to be most effective. Therefore, to further increase the stereoselectivity of the intramolecular alkylation reaction, we chose to evaluate substituted aminoindane derivatives, which were synthesized from the corresponding indanones by one-pot reductive amination with *tert*-butanesulfinamide (Scheme 2 and Scheme 3).[6]



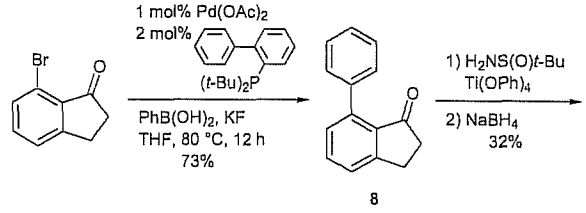
R = F, Me

4 R = F, 38%
5 R = Me, 24%

6 R = F
7 R = Me

Scheme 2 Asymmetric synthesis of chiral aminoindane derivatives **6** and **7**

Condensation of *tert*-butanesulfinamide with 7-fluoroindanone[7] and 7-methylindanone and subsequent reduction of the *N*-*tert*-butanesulfinyl imines with $NaBH_4$ provided sulfinamides **4** and **5** with dr > 99:1. The modest yields observed in these reactions are presumably the result of competing enamine formation in the imine condensation step (Scheme 2). Subsequent removal of the *tert*-butanesulfinyl group under acidic conditions provided the enantiomerically pure amines **6** and **7**.



Scheme 3 Asymmetric synthesis of chiral 7-phenylaminoindane **10**

For the introduction of a phenyl group in position 7 of the aminoindane, 7-bromo-aminoindanone[7] was subjected to Suzuki cross coupling under conditions described by Buchwald[8] to provide **8** in high yield (Scheme 3). Attempted condensation of ketone **8** with *tert*-butanesulfinamide using $Ti(OEt)_4$ resulted in Meerwein–Pondorf–Verley (MPV) reduction to give the undesired corresponding alcohol byproduct. Therefore, $Ti(OPh)_4$,[9] which is not capable of participating in MPV reduction, was used instead of $Ti(OEt)_4$ and provided sulfinamide **9** with high selectivity albeit in modest yield. Removal of the *tert*-butanesulfinyl group under acidic conditions gave enantiomerically pure amine **10**.

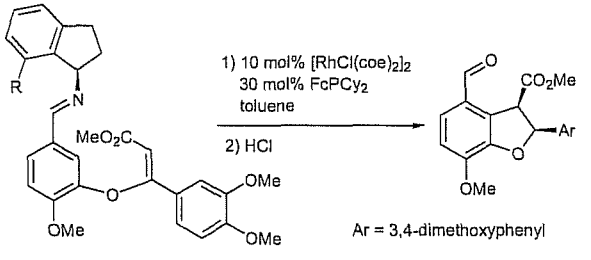
Each 7-substituted 2-aminoindane was condensed with aldehyde **1** to obtain the corresponding chiral imines **2** and **11–13**. Using optimized conditions with ferrocenyl-PCy_2 ($FcPCy_2$) as the ligand, the rhodium-catalyzed intramolecular alkylation led, after hydrolysis, to dihydrobenzofuran **3** with good yields and improved enantioselectivity (Table 1). The enantioselectivity provided by the 7-fluoroaminoindane chiral auxiliary at 90% ee was particularly impressive (entry 3).

We next focused our efforts on the asymmetric alkylation of substrates with different alkene substitution patterns to explore the scope of this method. Cyclization of substrates **14** and **15** with a phenyl group in place of the 3,4-dimethoxyphenyl group proceeded in good yields but with appreciable reduction in enantioselectivity (Table 2).

Imines **17–20** with 1,1- and 1,2-disubstituted double bonds, respectively, were also evaluated (Table 3). Conversion of the corresponding aldehyde into chiral imines **17** and **18** followed by cyclization provided dihydrofuran **21** in quantitative yield after auxiliary hydrolysis. Once again, 7-fluoro-aminoindane provided the highest enantiomeric excess (entry 2). In contrast, imines **19** and **20**, prepared from the 1,2-disubstituted aldehyde, cyclized significantly less efficiently, with product **22** being obtained in lower yield and with lower enantioselectivity (entries 3 and 4).

Additionally, asymmetric cyclization of an achiral imine through imine exchange[10] using catalytic amounts of chiral amine was investigated. Effective imine exchange was first demonstrated by cyclization of achiral *N*-*tert*-butyl aldimine **23** upon addition of one equivalent of chiral aminoindane (Table 4, entry 1). The enantiomeric purity of the product aldehyde **21** establishes that transimination

Table 1 Asymmetric Cyclization of Chiral Imines **2**, **11–13**

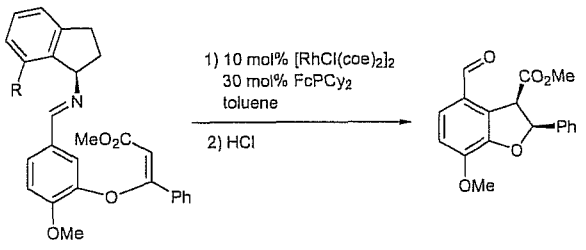


2, 11–13 3

Entry	Imine	R	Temp (°C)	Time (h)	Yield (%)	ee (%)[a]
1	**2**	H	75	16	76	76
2	**11**	Me	75	16	62	80
3	**12**	F	60	36	70[b]	90
4	**13**	Ph	75	16	90	83

[a] Enantiomeric excess determined by chiral HPLC after hydrolysis of imine with 1 M HCl (aq).
[b] Includes trace amounts of *trans* diastereomer.

Table 2 Asymmetric Cyclization of Chiral Imines **14** and **15**

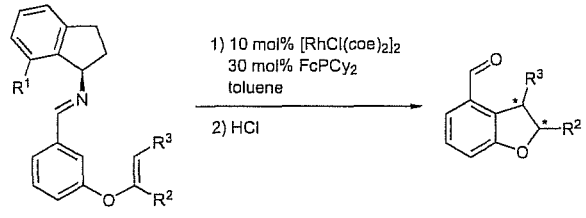


14, 15 16

Entry	Imine	R	Temp (°C)	Time (h)	Yield (%)	ee (%)[a]
1	**14**	H	75	16	80	65
2	**15**	F	75	16	81	70

[a] Enantiomeric excess determined by chiral HPLC after hydrolysis of imine with 1 M HCl (aq).

Table 3 Asymmetric Cyclization of Chiral Imines **17–20**

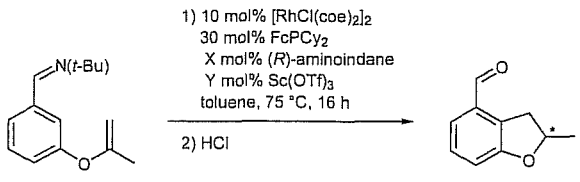


17–20 21, 22

Entry	Imine	R^1	R^2	R^3	Yield (%)[a]	ee (%)[b]	Product
1	**17**	H	Me	H	>99	58	**21**
2	**18**	F	Me	H	>99	68	**21**
3	**19**	H	H	Me	34	55	**22**
4	**20**	F	H	Me	50	58	**22**

[a] Yields based on ^{1}H NMR integration relative to 2,6-dimethoxytoluene as an internal standard.
[b] Enantiomeric excess determined by chiral HPLC after hydrolysis of imine with 1 M HCl (aq).

Table 4 Catalytic Asymmetric Cyclization of Achiral Imine **24** through Imine Exchange



23 **21**

Entry	Imine	X (mol%)	Y (mol%)	Yield (%)	ee (%)[a]
1	**23**	100	0	88	58
2	**23**	30	10	75	45

[a] Enantiomeric excess was determined by chiral HPLC after hydrolysis of imine with 1 M HCl (aq).

occurs considerably faster than cyclization of the sterically hindered achiral imine, which would lead to racemic product. Catalytic asymmetric cyclization of **23** was next demonstrated by addition of 30 mol% of chiral aminoindane along with 10 mol% $Sc(OTf)_3$, which was required to accelerate the imine exchange process. Only a minor drop in the yield and enantiomeric excess of product **22** was observed (entry 2).

In conclusion, asymmetric intramolecular alkylation of chiral aromatic aldimines was evaluated for differentially substituted alkene substrates. The highest enantioselectivities were obtained using the 7-fluoro-aminoindane as the chiral auxiliary with cyclization providing product in 90% ee for the most favorable substrate. Additionally, initial demonstration of catalytic asymmetric intramolecular alkylation was accomplished by employing a sterically hindered achiral imine substrate and catalytic amounts of a chiral amine.

Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. THF was distilled under N_2 from sodium benzophenone ketyl, pyridine from CaH_2, and MeOH from $Mg(MeO)_2$ immediately prior to use. Degassed toluene was purified by passage through an activated alumina column. All organic reactions were performed under an atmosphere of N_2 in flame-dried or oven-dried glassware unless otherwise stated. All C–H activation experiments were prepared in an N_2-filled Vac inert atmosphere box. The following compounds were prepared according to referenced literature procedures: $[RhCl(coe)_2]_2$[11] and $FcPCy_2$.[12] Thin-layer chromatography was performed on Merck 60 F254 250 μm silica gel plates. Visualization of the developed chromatogram was performed by fluorescence quenching, $KMnO_4$ stain, or *p*-anisaldehyde stain. Flash chromatography was carried out according to the general procedure of Still[13] using Merck 60 230–240 mesh silica gel or basic Al_2O_3 (activity grade I) as noted. Organic extracts were dried over $MgSO_4$ or Na_2SO_4 and were concentrated using a Büchi rotary evaporator under high vacuum pressure. Melting points were determined on a Mel-Temp apparatus and are uncorrected. Unless otherwise noted, ^1H NMR and ^{13}C NMR spectra were obtained in $CDCl_3$. NMR chemical shifts are reported in ppm and referenced to residual protonated solvent. Mass spectra were performed by the University of California, Berkeley Micro-Mass Facility. Chiral HPLC analyses were performed on an Agilent 1100 system with a Chiral PAK AS column (250 mm 4.6 mm) with a flow rate of 1 mL/min and with *i*-PrOH–hexanes as the mobile phase. A Perkin-Elmer 241 polarimeter with a sodium lamp was used to determine specific rotations and concentrations are reported in g/dL.

Imine Formation

To a 25 mL round-bottom flask equipped with a magnetic stir bar and septum was added 1.00 mmol of aldehyde, benzene (10 mL), MS 4 Å (1.0 g), and 1.1 equiv of amine (1.10 mmol). The reaction flask was then equipped with a reflux condenser, and the mixture was heated to reflux for 12 h. The reaction mixture was cooled to r.t., diluted with benzene, dried over Na_2SO_4, filtered, and concentrated.

Cyclization of Aromatic Imines

In a dry box, a solution of $[RhCl(coe)_2]_2$ (3.59 mg, 5 μmol, 0.1 equiv) and $FcPCy_2$ (5.73 mg, 15.0 μmol, 0.3 equiv) in toluene-d_8 (0.25 mL) was added to a solution of imine (50.0 μmol, 1.0 equiv) in toluene (0.25 mL) and then transferred to an NMR tube. The tube was sealed, and the solution was stirred at 75 °C for 16 h. The reaction solution was cooled to r.t., transferred to a round-bottom flask with EtOAc rinses, and concentrated under reduced pressure. The residue was washed with 1 N HCl (aq) and stirred for 20 min. The mixture was diluted with EtOAc, the layers were separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were dried, filtered, and concentrated under reduced pressure. The crude material was chromatographed on SiO_2.

Deprotection of *tert*-Butanesulfinamide Derivatives

To the *tert*-butanesulfinamide derivatives was added 1:1 (v/v) MeOH and HCl–dioxane solution (4 M, 3 equiv). The mixture was stirred at r.t. for 30 min and then concentrated to near dryness. The amine hydrochloride was precipitated in a mixture of MeOH and *tert*-butyl methyl ether. The precipitate was then filtered off and washed with *tert*-butyl methyl ether. The amine hydrochloride was dissolved in 1 N $NaHCO_3$ solution, which was subsequently extracted three times with EtOAc. The combined organic layers were dried over $MgSO_4$, filtrated, and concentrated to provide each amine in quantitative yields.

3-(3,4-Dimethoxyphenyl)-3-[5-(indan-1-yliminomethyl)-2-methoxyphenoxy]acrylic Acid Methyl Ester (2)

This compound was prepared according to the general procedure for imine formation with 1 equiv of aldehyde (18.6 mg, 0.0500 mmol) and 1.5 equiv of amine (7.32 mg, 0.0550 mmol). ^1H NMR (400 MHz, $CDCl_3$): δ = 8.18 (s, 1 H, C*H*=NCH), 7.38 (d, 1 H, *J* = 8.4 Hz, ArH), 7.31–7.11 (m, 6 H, ArH × 6), 7.00 (d, 1 H, *J* = 7.3 Hz, ArH), 6.90 (d, 1 H, *J* = 8.4 Hz, ArH), 6.73 (d, 1 H, *J* = 8.5 Hz, ArH), 5.97 (s, 1 H, C*H*CO_2CH_3), 4.78 (t, 1 H, *J* = 7.2 Hz, CH_2CHN=CH), 3.93 (s, 3 H, OCH_3), 3.79 (s, 3 H, OCH_3), 3.76 (s, 3 H, OCH_3), 3.64 (s, 3 H, CO_2CH_3), 3.07–3.01 (m, 1 H, one of ArCH_2CH_2), 2.92–2.84 (m, 1 H, one of ArCH_2CH_2), 2.39–2.35 (m, 1 H, one of $ArCH_2CH_2$), 2.19–2.09 (m, 1 H, one of $ArCH_2CH_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.6, 162.6, 159.0, 151.3, 150.8, 148.6, 146.0, 144.1, 143.4, 129.2, 128.0, 127.2, 126.0, 124.4, 124.0, 124.0, 120.5, 116.1, 111.6, 110.6, 109.5, 103.6, 74.5, 55.8, 55.5, 55.4, 50.9, 33.9, 30.7. $[\alpha]_D^{25}$ 7.7 (*c* 1.12, CH_2Cl_2). HRMS–FAB: *m/z* calcd for $C_{29}H_{30}NO_6$ $[M + H]^+$: 488.2073; found: 488.2079.

2-Methylpropane-2-sulfinic Acid (7-Fluoroindan-1-yl)amide (4)

To a 25 mL round-bottom flask equipped with a magnetic stir bar and septum were added 7-fluoroindan-1-one (190 mg, 1.23 mmol), 2 equiv of (*R*)-2-methylpropane-2-sulfinic acid amide (297 mg, 2.45 mmol), and 2.5 mL of THF. Under argon atmosphere, 4 equiv of $Ti(OEt)_4$ (1.12 g, 4.90 mmol) was added to the reaction mixture.

The reaction flask was then equipped with a reflux condenser and the mixture was heated to reflux for 12 h. The reaction mixture was cooled to –78 °C and 4 equiv of $NaBH_4$ (185 mg, 4.90 mmol) was added. The reaction mixture was stirred for 30 min at –78 °C and allowed to warm to r.t. The reaction mixture was quenched with NaCl solution, and the precipitate was filtered off and washed with EtOAc. After phase separation, the aqueous phase was extracted with EtOAc. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The crude material was chromatographed on SiO_2 (10–50% EtOAc–hexanes) to afford compound **4** as a yellow oil (120 mg, 0.470 mmol, 38%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.19–7.14 (m, 1 H, ArH), 6.97 (d, 1 H, *J* = 7.2 Hz, ArH), 6.81 (t, 1 H, *J* = 8.8 Hz, ArH), 5.08–5.05 (m, 1 H, HNC*H*$_2$CH$_2$), 3.76 [br s, 1 H, NHS(O)*t*-Bu], 3.11–3.03 (m, 1 H, one of ArC*H*$_2$CH$_2$), 2.86–2.79 (m, 1 H, one of ArC*H*$_2$CH$_2$), 2.44–2.35 (m, 1 H, one of ArCH$_2$C*H*$_2$), 2.19–2.11 (m, 1 H, one of ArCH$_2$C*H*$_2$), 1.12 [s, 9 H, C(CH$_3$)$_3$]. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.5, 158.0, 147.5, 147.4, 130.1, 130.1, 128.9, 128.8, 120.5, 120.4, 113.2, 113.0, 56.7, 56.7, 55.3, 33.3, 30.6, 30.6, 22.2 (multiple C's coupled to F). $[\alpha]_D^{25}$ –6.1 (*c* 2.8, CH_2Cl_2). HRMS–FAB: *m/z* calcd for $C_{13}H_{19}FNOS$ $[M + H]^+$: 256.1171; found: 256.1171.

Propane-2-sulfinic Acid (7-Methylindan-1-yl)amide (5)

To a 25 mL round-bottom flask equipped with a magnetic stir bar and septum were added 7-methylindan-1-one (179 mg, 1.23 mmol), 2 equiv of (*R*)-2-methylpropane-2-sulfinic acid amide (297 mg, 2.45 mmol), and 2.5 mL of THF. Under argon atmosphere, 4 equiv of $Ti(OEt)_4$ (1.12 g, 4.90 mmol) was added to the reaction mixture. The reaction flask was then equipped with a reflux condenser and the mixture was heated to reflux for 12 h. The reaction mixture was cooled to –78 °C and 4 equiv of $NaBH_4$ (185.4 mg, 4.90 mmol) was added. The reaction mixture was stirred for 30 min at –78 °C and allowed to warm to r.t. The reaction mixture was quenched with NaCl solution, and the precipitate was filtered off and washed with EtOAc. After phase separation, the aqueous phase was extracted with EtOAc. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The crude material was chromatographed on SiO_2 (10–50% EtOAc–hexanes) to afford compound **5** as a white solid (73.9 mg, 0.294 mmol, 24%); mp 67–68 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.17 (t, 1 H, *J* = 7.2 Hz, ArH), 7.08 (d, 1 H, *J* = 7.6 Hz, ArH), 6.99 (d, 1 H, *J* = 7.2 Hz, ArH), 4.94 (br s, 1 H, HNC*H*CH$_2$CH$_2$), 3.18–3.09 [m, 2 H, NHS(O)*t*-Bu, one of ArC*H*$_2$CH$_2$], 2.83–2.77 (m, 1 H, one of ArC*H*$_2$CH$_2$), 2.37 (s, 3 H, ArCH$_3$), 2.21–2.16 (m, 2 H, ArCH$_2$C*H*$_2$), 1.15 [s, 9 H, C(CH$_3$)$_3$]. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.0, 141.3, 134.5, 128.8, 128.0, 122.2, 58.2, 55.3, 33.6, 30.3, 22.4, 18.4. $[\alpha]_D^{25}$ –9.2 (*c* 1.5, CH_2Cl_2). HRMS–FAB: *m/z* calcd for $C_{14}H_{22}NOS$ $[M + H]^+$: 252.1422; found: 252.1422.

Amines **6** and **7** were prepared according to the general procedure for the deprotection of *tert*-butanesulfinamide derivatives.

7-Fluoroindan-1-ylamine (6)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.18–7.11 (m, 1 H, ArH), 6.96 (d, 1 H, *J* = 10.0 Hz, ArH), 6.82 (t, 1 H, *J* = 12.0 Hz, ArH), 4.63 (t, 1 H, *J* = 8.4 Hz, H$_2$NC*H*CH$_2$), 3.08–3.01 (m, 1 H, one of ArC*H*$_2$CH$_2$), 2.86–2.76 (m, 1 H, one of ArC*H*$_2$CH$_2$), 2.25–2.41 (m, 1 H, one of ArCH$_2$C*H*$_2$), 1.95–1.75 (m, 3 H, one of ArCH$_2$C*H*$_2$, NH$_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.2, 158.7, 146.7, 146.6, 133.3, 133.1, 129.3, 129.2, 120.5, 113.2, 113.0, 55.0, 35.5, 30.6 (multiple Cs coupled to F). $[\alpha]_D^{25}$ –0.4 (*c* 3.5, CH_2Cl_2).

7-Methylindan-1-ylamine (7)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.17–7.05 (m, 2 H, ArH × 2), 6.99 (d, 1 H, *J* = 9.2 Hz, ArH), 4.50–4.46 (dd, 1 H, *J* = 9.6, 3.6 Hz, H$_2$NC*H*CH$_2$), 3.17–3.06 (m, 1 H, one of ArC*H*$_2$CH$_2$), 2.84–2.75 (m, 1 H, one of ArC*H*$_2$CH$_2$), 2.40 (s, 3 H, ArCH$_3$), 2.40–2.29 (m, 1 H, one of ArCH$_2$C*H*$_2$), 1.96–1.88 (m, 1 H, one of ArCH$_2$C*H*$_2$), 1.55 (br s, 2 H, NH$_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.3, 143.2, 133.9, 127.9, 127.7, 122.3, 55.9, 35.7, 30.2, 18.4. $[\alpha]_D^{25}$ –2.08 (*c* 0.5, CH_2Cl_2).

7-Phenylindan-1-one (8)

In a dry box, 7-bromoindan-1-one (105 mg, 0.500 mmol), 3 equiv of KF (87.2 mg, 1.50 mmol), 1.5 equiv of phenylboronic acid (91.5 mg, 0.750 mmol), 1 mol% of $Pd(OAc)_2$ (1.1 mg, 0.0050 mmol), 2 mol% of biphP(*t*-Bu)$_2$ (3.0 mg, 0.010 mmol), and 0.5 mL of THF were added to a Schlenk flask. The flask was sealed, and the solution was stirred at 80 °C for 14 h. The reaction solution was cooled to r.t., diluted with EtOAc, and washed with brine and H_2O. The aqueous layer was extracted with EtOAc, and the combined organic layers were dried, filtered, and concentrated under reduced pressure. The crude material was chromatographed on SiO_2 (0–10% EtOAc–hexanes) to afford compound **8** as a white solid (76.0 mg, 0.365 mmol, 73%); mp 91–92 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.60 (t, 1 H, *J* = 7.6 Hz, ArH), 7.52–7.41 (m, 6 H, ArH × 6), 7.28 (d, 1 H, *J* = 7.6 Hz, ArH), 3.16–3.13 (m, 2 H, ArC*H*$_2$CH$_2$), 2.71–2.68 (m, 2 H, ArCH$_2$C*H*$_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 205.2, 156.1, 141.1, 137.8, 133.6, 132.7, 129.1, 129.1, 127.5, 127.4, 125.5, 36.6, 25.0. HRMS–FAB: *m/z* calcd for $C_{15}H_{13}O$ $[M + H]^+$: 209.0966; found: 209.0966.

2-Methylpropane-2-sulfinic Acid (7-phenylindan-1-yl)amide (9)

To a 25 mL round-bottom flask equipped with a magnetic stir bar and septum were added 7-phenylindan-1-one (200 mg, 0.960 mmol), 2 equiv of (*R*)-2-methylpropane-2-sulfinic acid amide (233 mg, 1.92 mmol), and 2.5 mL of THF. Under an argon atmosphere, 4 equiv of $Ti(OPh)_4$ (1.61 g, 3.84 mmol) was added to the reaction mixture. The reaction flask was then equipped with a reflux condenser, and the mixture was heated to reflux for 12 h. The reaction mixture was then cooled to –78 °C, and 4 equiv of $NaBH_4$ (145 mg, 3.84 mmol) were added. The reaction mixture was stirred for 30 min at –78 °C and allowed to warm to r.t. The reaction mixture was quenched with NaCl solution, and the precipitate was filtered off and washed with EtOAc. After phase separation, the aqueous phase was extracted with EtOAc. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The crude material was chromatographed on SiO_2 (10–40% EtOAc–hexanes) to afford compound **9** as a white solid (95.0 mg, 0.303 mmol, 32%); mp 109–110 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.51–7.45 (m, 4 H, ArH × 4), 7.36–7.41 (m, 1 H, ArH), 7.33 (d, 1 H, *J* = 7.6 Hz, ArH), 7.27–7.29 (m, 1 H, ArH), 7.18 (d, 1 H, *J* = 7.2 Hz, ArH), 5.29 (t, 1 H, *J* = 6.0 Hz, HNC*H*CH$_2$), 3.42 [s, 1 H, NHS(O)*t*-Bu], 3.14–3.08 (m, 1 H, one of ArC*H*$_2$CH$_2$), 3.01–2.93 (m, 1 H, one of ArC*H*$_2$CH$_2$), 2.60–2.53 (m, 1 H, one of ArCH$_2$C*H*$_2$), 2.14–2.07 (m, 1 H, one of ArCH$_2$C*H*$_2$), 0.89 [s, 9 H, C(CH$_3$)$_3$]. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.8, 140.4, 139.7, 138.6, 129.0, 128.4, 128.4, 127.8, 127.8, 124.0, 57.3, 54.8, 32.7, 30.5, 22.1. $[\alpha]_D^{25}$ –16.8 (*c* 0.6, CH_2Cl_2). HRMS–FAB: *m/z* calcd for $C_{19}H_{24}NOS$ $[M]^+$: 314.1579; found: 314.1579.

7-Phenylindan-1-ylamine (10)

This compound was prepared according to the general procedure for the deprotection of *tert*-butanesulfinamide derivatives. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.44 (m, 4 H, ArH × 4), 7.38–7.36 (m, 1 H, ArH), 7.31–7.22 (m, 2 H, ArH × 2), 7.07 (d, 1 H, *J* = 10.0 Hz, ArH), 4.74 (t, 1 H, *J* = 8.4 Hz, H$_2$NC*H*CH$_2$), 3.14–3.08 (m, 1 H, one of ArC*H*$_2$CH$_2$), 3.13–3.03 (m, 1 H, one of ArC*H*$_2$CH$_2$), 2.94–2.84 (m, 1 H, one of ArC*H*$_2$CH$_2$), 2.54–2.43 (m, 1 H, one of ArCH$_2$C*H*$_2$), 1.81–1.70 (m, 1 H, one of ArCH$_2$C*H*$_2$), 1.47 (br s, 2 H, NH$_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.9, 140.8, 138.7, 128.6, 128.3, 127.8, 127.7, 127.2, 124.0, 56.1, 35.2, 30.2. $[\alpha]_D^{25}$ –3.5 (*c* 3.5, CH_2Cl_2).

3-(3,4-Dimethoxyphenyl)-3-{2-methoxy-5-[(7-methylindan-1-ylimino)methyl]phenoxy}acrylic Acid Methyl Ester (11)

This compound was prepared according to the general procedure for imine synthesis with 1 equiv of aldehyde (18.6 mg, 0.0500 mmol) and 1.5 equiv of amine (8.1 mg, 0.0550 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.08 (s, 1 H, C*H*=NCH), 7.33 (d, 1 H, *J* = 8.5 Hz, ArH), 7.20–7.18 (m, 2 H, ArH × 2), 7.15–7.09 (m, 3 H, ArH × 3), 6.94 (d, 1 H, *J* = 7.0 Hz, ArH), 6.80 (d, 1 H, *J* = 8.5 Hz, ArH), 6.77 (d, 1 H, *J* = 8.5 Hz, ArH), 5.96 (s, 1 H, C*H*CO_2CH_3), 4.98–4.95 (m, 1 H, CH_2CHN=CH), 3.96 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 3.79 (s, 3 H, OCH_3), 3.67 (s, 3 H, CO_2CH_3), 3.14–3.10 (m, 1 H, one of ArCH_2CH_2), 2.89–2.86 (m, 1 H, one of ArCH_2CH_2), 2.39–2.34 (m, 1 H, one of ArCH_2CH_2), 2.10 (s, 3 H, $ArCH_3$), 2.06–2.02 (m, 1 H, one of ArCH_2CH_2). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.0, 162.9, 158.2, 151.4, 151.0, 148.8, 146.2, 144.6, 142.0, 135.4, 129.6, 128.3, 127.9, 127.8, 126.4, 124.1, 122.2, 120.7, 116.3, 111.8, 110.8, 109.8, 103.9, 73.7, 56.1, 55.9, 55.7, 51.2, 33.9, 31.0, 18.8. $[\alpha]_D^{25}$ +4.2 (*c* 2.0, CH_2Cl_2).

3-(3,4-Dimethoxyphenyl)-3-{5-[(7-fluoroindan-1-ylimino)methyl]-2-methoxyphenoxy}acrylic Acid Methyl Ester (12)

In a dry box, 1 equiv of aldehyde (20.8 mg, 0.0559 mmol), 1.1 equiv of amine (9.3 mg, 0.0615 mmol), and 0.5 mL of benzene were combined in a vial and stirred overnight at r.t. The resulting reaction mixture was diluted with 2 mL of Et_2O, filtered through Celite, and concentrated to yield a colorless oil (28.0 mg, 0.0554 mmol, 99%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.16 (s, 1 H, C*H*=NCH), 7.38–7.36 (m, 2 H, ArH × 2), 7.27–7.10 (m, 3 H, ArH × 3), 7.04 (d, 1 H, *J* = 7.2 Hz, ArH), 6.90 (d, 1 H, *J* = 8.4 Hz, ArH), 6.82–6.76 (m, 2 H, ArH × 2), 5.96 (s, 1 H, C*H*CO_2CH_3), 5.05 (m, 1 H, CH_2CHN=CH), 3.95 (s, 3 H, OCH_3), 3.87 (s, 3 H, OCH_3), 3.79 (s, 3 H, OCH_3), 3.67 (s, 3 H, CO_2CH_3), 3.21–3.17 (m, 1 H, one of ArCH_2CH_2), 2.95–2.85 (m, 1 H, one of ArCH_2CH_2), 2.45–2.35 (m, 1 H, one of ArCH_2CH_2), 2.25–2.15 (m, 1 H, one of ArCH_2CH_2). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.0, 163.0, 161.6, 159.1, 151.4, 151.0, 148.7, 148.1, 148.0, 146.1, 130.1, 130.0, 129.7, 129.7, 129.5, 128.3, 126.3, 124.0, 120.7, 120.4, 120.4, 116.7, 113.2, 113.0, 111.8, 110.8, 109.7, 103.7, 71.6, 71.6, 56.1, 56.0, 55.9, 55.8, 55.7, 51.2, 34.0, 31.4 (multiple C's coupled to F).

3-(3,4-Dimethoxyphenyl)-3-{2-methoxy-5-[(7-phenylindan-1-ylimino)methyl]phenoxy}acrylic Acid Methyl Ester (13)

This compound was prepared according the general procedure for imine synthesis with 1 equiv of aldehyde (18.6 mg, 0.0500 mmol) and 1.5 equiv of amine (11.5 mg, 0.0550 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.05 (m, 13 H, ArH × 12, C*H*=NCH), 6.83 (m, 2 H, ArH × 2), 5.96 (s, 1 H, C*H*CO_2CH_3), 4.93 (m, 1 H, CH_2CHN=CH), 3.94 (s, 3 H, OCH_3), 3.87 (s, 3 H, OCH_3), 3.79 (s, 3 H, OCH_3), 3.69 (s, 3 H, CO_2CH_3), 3.20–3.18 (m, 1 H, one of ArCH_2CH_2), 3.00–2.90 (m, 1 H, one of ArCH_2CH_2), 2.41–2.32 (m, 1 H, one of ArCH_2CH_2), 2.15–2.00 (m, 1 H, one of ArCH_2CH_2). $[\alpha]_D^{25}$ +7.7 (*c* 1.5, CH_2Cl_2).

2-(3,4-Dimethoxyphenyl)-4-formyl-7-methoxy-2,3-dihydrobenzofuran-3-carboxylic Acid Methyl Ester (3)

The C–H activation reactions of imines **2** and **11–13** were performed following the general procedure for the cyclization of aromatic imines. The crude material was chromatographed on SiO_2 (2–50% EtOAc–hexanes) to afford compound **6** as a white solid with yields and ee as described in the text. The ee was determined by HPLC analysis; mp 119–120 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.82 (s, 1 H, CHO), 7.39 (d, 1 H, *J* = 8.3 Hz, ArH), 6.98 (d, 1 H, *J* = 8.3 Hz, ArH), 6.96–6.62 (m, 2 H, ArH × 2), 6.82 (d, 1 H, *J* = 8.2, ArH), 6.00 (d, 1 H, *J* = 10.2 Hz, ArOCHAr), 4.89 (d, 1 H, *J* = 10.2 Hz, ArC*H*CO_2CH_3), 3.97 (s, 3 H, OCH_3), 3.85 (s, 3 H, OCH_3), 3.84 (s, 3 H, OCH_3), 3.23 (s, 3 H, CO_2CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.6, 169.7, 149.9, 149.5, 149.0, 148.5, 128.7, 128.2, 126.4, 125.3, 119.4, 111.5, 110.3, 109.4, 87.7, 56.0, 55.8, 55.7, 54.1, 51.7. $[\alpha]_D^{25}$ –112.9 (*c* 0.95, CH_2Cl_2). HRMS–FAB: *m/z* calcd for $C_{20}H_{20}O_7$ $[M]^+$: 372.1209; found: 372.1213. HPLC analysis [AS column, hexanes–*i*-PrOH (70:30), 40 min run time]: peak 1, t_R = 16.6 min (minor enantiomer) and peak 2, t_R = 31.0 min (major enantiomer).

3-(3-Formylphenoxy)-3-phenylacrylic Acid Methyl Ester

To a sealed tube equipped with a magnetic stir bar was added MeOH (42 mL) followed by Na metal (1.58 g, 68.8 mmol, 1.6 equiv, cut into small pieces). Once all the Na had dissolved, isovanillin (48.4 g, 318 mmol, 7.6 equiv) was added, and the reaction mixture became a thick, yellow slurry. After stirring at r.t. for 5 min, pyridine (42 mL) was added, followed by phenylpropynoic acid methyl ester (5.00 g, 43.0 mmol, 1.0 equiv), and the reaction mixture was stirred at 120 °C for 1.75 h. The mixture was cooled to r.t., diluted with EtOAc, and sat. aq NH_4Cl solution was added. The layers were separated, and the organic layer was washed several times with sat. aq K_2CO_3 solution to remove excess isovanillin. The combined organic layers were dried, filtered, and concentrated under reduced pressure. The crude material was chromatographed on basic alumina (0–20% EtOAc–hexane) to afford the *Z*-alkene as a white solid (5.20 g, 18.4 mmol, 42%); mp 98–99 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.68 (s, 1 H, CHO), 7.57 (dd, 2 H, *J* = 2.0, 6.4 Hz, ArH), 7.45 (dd, 1 H, *J* = 2.0, 8.4 Hz, ArH), 7.35–7.25 (m, 4 H, *J* = 2.0 Hz, ArH), 7.00 (d, 1 H, *J* = 8.4 Hz, ArH), 6.15 (s, 1 H, $CHCO_2Me$), 4.00 (s, 3 H, OCH_3), 3.64 (s, 3 H, OCH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.2, 164.3, 162.1, 154.4, 146.5, 133.1, 130.8, 129.7, 128.7, 127.5, 126.8, 114.9, 111.5, 105.8, 56.2, 51.2. HRMS–FAB: *m/z* calcd for $C_{18}H_{17}O_5$ $[M + H]^+$: 313.1076; found: 313.1076.

3-[5-(Indan-1-yliminomethyl)-2-methoxyphenoxy]-3-phenylacrylic Acid Methyl Esters (14)

This compound was prepared according to the general procedure for imine synthesis with 1 equiv of aldehyde (14.1 mg, 0.0500 mmol) and 1.5 equiv of amine (7.3 mg, 0.0550 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20 (s, 1 H, C*H*=NCH), 7.59 (d, 2 H, *J* = 7.6 Hz, ArH × 2), 7.43 (d, 1 H, *J* = 8.0 Hz, ArH), 7.37–7.32 (m, 3 H, ArH × 3), 7.20–7.16 (m, 4 H, ArH × 4), 7.02 (d, 1 H, *J* = 7.6 Hz, ArH), 6.93 (d, 1 H, *J* = 8.4 Hz, ArH), 6.05 (s, 1 H, C*H*CO_2CH_3), 4.81 (t, 1 H, *J* = 7.2 Hz, CH_2CHN=CH), 3.98 (s, 3 H, OCH_3), 3.68 (s, 3 H, OCH_3), 3.12–3.07 (m, 1 H, one of ArCH_2CH_2), 2.94–2.88 (m, 1 H, one of ArCH_2CH_2), 2.45–2.39 (m, 1 H, one of ArCH_2CH_2), 2.20–2.15 (m, 1 H, one of ArCH_2CH_2). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.9, 163.0, 159.1, 151.4, 148.1, 146.0, 133.9, 130.5, 129.7, 129.4, 128.6, 127.1, 123.9, 120.4, 120.4, 116.6, 113.2, 113.1, 112.0, 105.1, 71.6, 56.2, 51.3, 34.1, 31.4. $[\alpha]_D^{25}$ +1.3 (*c* 2.9, CH_2Cl_2).

3-{5-[(7-Fluoroindan-1-ylimino)methyl]-2-methoxyphenoxy}-3-phenylacrylic Acid Methyl Ester (15)

This compound was prepared according to the general procedure for imine synthesis with 1 equiv of aldehyde (14.1 mg, 0.0500 mmol) and 1.5 equiv of amine (8.3 mg, 0.0550 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12 (s, 1 H, C*H*=NCH), 7.59 (d, 2 H, *J* = 6.8 Hz, ArH × 2), 7.36–7.27 (m, 4 H, ArH × 4), 7.18–7.13 (m, 2 H, ArH × 2), 7.02 (d, 1 H, *J* = 5.6 Hz, ArH), 6.87 (d, 1 H, *J* = 6.8 Hz, ArH), 6.78 (t, 1 H, *J* = 6.8 Hz, ArH), 6.00 (s, 1 H, C*H*CO_2CH_3), 5.03 (m, 1 H, CH_2CHN=CH), 3.92 (s, 3 H, OCH_3), 3.65 (s, 3 H, OCH_3), 3.20–3.14 (m, 1 H, one of ArCH_2CH_2), 2.89–2.85 (m, 1 H, one of ArCH_2CH_2), 2.40–2.36 (m, 1 H, one of ArCH_2CH_2), 2.17–2.14 (m, 1 H, one of ArCH_2CH_2). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.8, 162.9, 159.4, 151.5, 146.1, 144.4, 143.7, 130.6, 129.4, 128.6, 127.4, 127.1, 126.3, 124.7, 124.3, 123.9, 116.4, 111.9, 105.3, 74.7, 56.2, 51.3, 34.2, 30.9 (multiple C's coupled to F). $[\alpha]_D^{25}$ +1.8 (*c* 1.1, CH_2Cl_2).

7-Formyl-4-methoxy-2-phenylindan-1-carboxylic Acid Methyl Ester (16)

The C–H activation reactions of imines **14** and **15** were performed following the general procedure for the cyclization of aromatic imines. The crude material was chromatographed on SiO_2 (2–30% EtOAc–hexanes) to afford compound **16** as a white solid with yields and ee as described in the text. The ee was determined by HPLC analysis; mp 135–136 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.82 (s, 1 H, CHO), 7.41–7.28 (m, 6 H, ArH × 6), 6.99 (d, 1 H, *J* = 8.4 Hz, ArH), 6.07 (d, 1 H, *J* = 10.4 Hz, ArOCHAr), 4.95 (d, 1 H, *J* = 10.0 Hz, ArC*H*CO_2CH_3), 3.97 (s, 3 H, OCH_3), 3.13 (s, 3 H, OCH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.7, 169.5, 150.4, 149.6, 136.0, 128.8, 128.51, 128.1, 126.6, 126.5, 125.3, 111.7, 87.8, 56.2, 54.3, 51.6. HRMS–FAB: *m/z* calcd for $C_{18}H_{16}O_5$ $[M]^+$: 312.0998; found: 312.0998. HPLC analysis [AS column, hexane–*i*-PrOH (75:25), 45 min run time]: peak 1, t_R = 10.8 min (minor enantiomer) and peak 2, t_R = 20.0 min (major enantiomer).

3-Isopropenyloxybenzaldehyde

To a 100 mL round-bottom flask equipped with a magnetic stir bar and septum were added 1.5 equiv (7.98 g, 24.6 mmol) of Cs_2CO_3, 0.25 equiv of CuCl (405 mg, 4.10 mmol), 0.5 equiv of acetylacetone (819 mg, 8.19 mmol), and 50 mL of THF. The suspension was stirred for 5 min at r.t. Under an argon atmosphere, 3-hydroxybenzaldehyde (2.0 g, 16.38 mmol) and 1.3 equiv of 2-bromopropene (1.86 mL, 21.29 mmol) were added to the reaction mixture. The reaction flask was then equipped with a reflux condenser, and the mixture was heated to reflux for 12 h. The reaction mixture was cooled to r.t., filtered, and concentrated under reduced pressure. The crude material was chromatographed on SiO_2 (0–10% EtOAc–hexanes) to afford the title compound as a yellow oil (690 mg, 4.26 mmol, 26%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.92 (s, 1 H, CHO), 7.56 (dd, 1 H, *J* = 1.2, 10.0 Hz, ArH), 7.49 (t, 1 H, *J* = 1.6 Hz, ArH), 7.44 (t, 1 H, *J* = 7.6 Hz, ArH), 7.24 (dd, 1 H, *J* = 1.2, 10.8 Hz, ArH), 4.23 (d, 1 H, *J* = 2.0 Hz, CH_2=CCH_3), 3.99 (d, 1 H, *J* = 2.0 Hz, CH_2=CCH_3), 1.93 (s, 3 H, CH_2=CCH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.3, 158.7, 156.0, 137.8, 130.0, 126.4, 125.2, 120.1, 91.5, 19.5. HRMS–FAB: *m/z* calcd for $C_{10}H_{10}O_2$ $[M]^+$: 162.0681; found: 162.0681.

3-Propenyloxybenzaldehyde

To a 100 mL round-bottom flask equipped with a magnetic stir bar and septum were added 1.5 equiv (7.98 g, 24.6 mmol) of Cs_2CO_3, 0.25 equiv of CuCl (405 mg, 4.10 mmol), 0.5 equiv of acetylacetone (819 mg, 8.19 mmol), and 50 mL of THF. The suspension was stirred for 5 min at r.t. Under an argon atmosphere, 1 equiv of 3-[1,3]dioxolan-2-yl-phenol (2.72 g, 16.38 mmol) and 1.5 equiv of 1-bromopropene were added to the reaction mixture. The reaction flask was then equipped with a reflux condenser and the mixture was heated to reflux for 12 h. The reaction mixture was cooled to r.t., filtered, and concentrated under reduced pressure. The acetal was hydrolyzed by stirring in 6 N HCl–MeOH for 1 h. The mixture was extracted with EtOAc and concentrated, and the crude material was chromatographed on SiO_2 (0–10% EtOAc–hexanes) to afford the *E*-alkene as a yellow oil (584 mg, 3.60 mmol, 22%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.90 (s, 1H, CHO), 7.45 (dd, 1 H, *J* = 1.2, 8.0 Hz, ArH), 7.41–7.37 (m, 2 H, ArH), 7.16 (dd, 1 H, *J* = 1.2, 5.2 Hz, ArH), 6.40–6.35 (m, 1 H, CH_3C*H*=CH), 5.42–5.34 (m, 1 H, CH_3CH=C*H*), 1.63 (dd, 3 H, *J* = 1.6, 6.8 Hz, C*H*$_3$CH=CH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.6, 157.8, 140.9, 137.7, 130.1, 124.4, 122.6, 114.9, 109.9, 12.1. HRMS–FAB(+): *m/z* calcd for $C_{10}H_{10}O_2$ $[M]^+$: 162.0681; found: 162.0680.

Imines **17**–**20** were prepared according to the general procedure for imine synthesis.

Indan-1-yl-(3-isopropenyloxybenzylidene)amine (17)

One equiv of aldehyde (8.1 mg, 0.0500 mmol) and 1.5 equiv of amine (7.32 mg, 0.0550 mmol) were condensed. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.43 (s, 1 H, C*H*=NCH), 7.55 (d, 1 H, *J* = 7.6 Hz, ArH), 7.51 (s, 1 H, ArH), 7.39 (t, 1 H, *J* = 8.0 Hz, ArH), 7.30 (d, 1 H, *J* = 7.2 Hz, ArH), 7.26–7.13 (m, 2 H, ArH × 2), 7.12 (m, 2 H, ArH × 2), 4.95 (t, 1 H, *J* = 7.2 Hz, CH_2C*H*N=CH), 4.21 [s, 1 H, one of CH_2=C(O)CH_3], 4.01 [s, 1 H, one of CH_2=C(O)CH_3], 3.18–3.12 (m, 1 H, one of ArCH_2CH_2), 3.02–2.94 (m, 1 H, one of ArCH_2CH_2), 2.53–2.47 (m, 1 H, one of ArCH_2CH_2), 2.32–2.23 (m, 1 H, one of ArCH_2CH_2), 2.00 (s, 3 H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.8, 159.4, 155.7, 144.1, 143.8, 138.0, 129.6, 127.6, 126.4, 124.8, 124.3, 124.0, 123.0, 120.1, 90.3, 74.9, 34.2, 31.0, 20.0. $[\alpha]_D^{25}$ +14.6 (*c* 1.0, CH_2Cl_2).

(7-Fluoroindan-1-yl)-(3-isopropenyloxybenzylidene)amine (18)

One equiv of aldehyde (8.3 mg, 0.0500 mmol) and 1.5 equiv of amine (7.3 mg, 0.0550 mmol) were condensed. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.48 (s, 1 H, C*H*=NCH), 7.50–7.43 (m, 2 H, ArH × 2), 7.34 (t, 1 H, *J* = 10.4 Hz, ArH), 7.25–7.17 (m, 1 H, ArH), 7.09–7.05 (m, 2 H, ArH × 2), 6.82 (t, 1 H, *J* = 11.2 Hz, ArH), 5.17–5.15 (m, 1 H, CH_2C*H*N=CH), 4.17 [s, 1 H, one of CH_2=C(O)CH_3], 3.97 [s, 1 H, one of CH_2=C(O)CH_3], 3.30–3.20 (m, 1 H, one of ArCH_2CH_2), 2.99–2.89 (m, 1 H, one of ArCH_2CH_2), 2.51–2.41 (m, 1 H, one of ArCH_2CH_2), 2.29–2.23 (m, 1 H, one of ArCH_2CH_2), 1.97 (s, 3 H, CH_3). $[\alpha]_D^{25}$ +2.2 (*c* 1.3, CH_2Cl_2).

Indan-1-yl-(3-propenyloxybenzylidene)amine (19)

One equiv of aldehyde (8.1 mg, 0.0500 mmol) and 1.5 equiv of amine (7.3 mg, 0.0550 mmol) were condensed. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.43 (s, 1 H, C*H*=NCH), 7.49 (s, 1 H, ArH), 7.43 (d, 1 H, *J* = 6.0 Hz, ArH), 7.36 (t, 1 H, *J* = 6.0 Hz, ArH), 7.32 (d, 1 H, *J* = 5.6 Hz, ArH), 7.26 (t, 1 H, *J* = 5.2 Hz, ArH), 7.21 (t, 1 H, *J* = 6.0 Hz, ArH), 7.12 (d, 1 H, *J* = 5.6 Hz, ArH), 7.07 (d, 1 H, *J* = 6.0 Hz, ArH), 6.49 [d, 1 H, *J* = 9.6 Hz, HC(CH_3)=C*H*OAr], 5.45–5.38 [m, 1 H, *H*C(CH_3)=CHOAr], 4.96 (t, 1 H, *J* = 5.6 Hz, CH_2C*H*N=CH), 3.18–3.13 (m, 1 H, one of ArCH_2CH_2), 3.02–2.96 (m, 1 H, one of ArCH_2CH_2), 2.51–2.49 (m, 1 H, one of ArCH_2CH_2), 2.33–2.26 (m, 1 H, one of ArCH_2CH_2), 1.69 (d, 3 H, *J* = 5.6 Hz, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.0, 157.7, 144.1, 143.8, 141.7, 137.8, 129.7, 127.6, 126.4, 124.8, 124.3, 123.0, 119.1, 114.6, 108.7, 74.9, 34.2, 31.0, 12.2. $[\alpha]_D^{25}$ +2.1 (*c* 1.9, CH_2Cl_2).

(7-Fluoroindan-1-yl)-(3-propenyloxybenzylidene)amine (20)

One equiv of aldehyde (8.11 mg, 0.05 mmol) and 1.5 equiv of amine (8.31 mg, 0.055 mmol) were condensed. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.39 (s, 1 H, C*H*=NCH), 7.40–7.37 (m, 2 H, ArH × 2), 7.32 (t, 1 H, *J* = 7.6 Hz, ArH), 7.25–7.16 (m, 1 H, ArH), 7.08 (d, 1 H, *J* = 7.2 Hz, ArH), 7.02 (d, 1 H, *J* = 8.0 Hz, ArH), 6.84 (t, 1 H, *J* = 8.8 Hz, ArH), 6.46 [d, 1 H, *J* = 12.4 Hz, HC(CH_3)=C*H*OAr], 5.41–5.36 [m, 1 H, *H*C(CH_3)=CHOAr], 5.18–5.17 (m, 1 H, CH_2C*H*N=CH), 3.31–3.23 (m, 1 H, one of ArCH_2CH_2), 2.98–2.97 (m, 1 H, one of ArCH_2CH_2), 2.52–2.47 (m, 1 H, one of ArCH_2CH_2), 2.29–2.28 (m, 1 H, one of ArCH_2CH_2), 1.68 [d, 3 H, *J* = 6.8 Hz, C(CH_3)$_3$]. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.9, 159.2, 157.7, 148.2, 148.1, 141.7, 137.9, 130.0, 129.9, 129.9, 129.6, 122.9, 120.5, 120.5, 119.0, 114.8, 113.3, 113.1, 108.6, 71.8, 34.1, 31.5, 31.5, 12.3 (multiple C's coupled to F). $[\alpha]_D^{25}$ +6.0 (*c* 1.0, CH_2Cl_2).

The C–H activation reactions of imines **17**–**20** were prepared following the general procedure for the cyclization of aromatic imines. The crude material was chromatographed on SiO_2 (0–1% EtOAc–hexanes) to afford compounds **21** and **22** as colorless oils with yields and ee as described in the text. The ee was determined by HPLC analysis.

2-Methyl-2,3-dihydrobenzofuran-4-carbaldehyde (21)
^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.03 (s, 1 H, CHO), 7.30–7.26 (m, 2 H, ArH × 2), 7.01–6.98 (m, 1 H, ArH), 5.06–4.97 [m, 1 H, $CH_3CH(CH_2)OAr$], 3.70–3.64 [dd, 1 H, J = 17.6, 8.8 Hz, one of $CH_3CH(CH_2)OAr$], 3.15–3.09 [dd, 1 H, J = 17.6, 7.6 Hz, one of $CH_3CH(CH_2)OAr$], 1.48 (d, 3 H, J = 6.0 Hz, CH_3CH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.5, 160.6, 132.9, 128.5, 128.0, 124.1, 114.7, 80.7, 36.8, 21.8. HPLC analysis [AS column, hexanes–*i*-PrOH (99:1), 20 min run time]: peak 1, t_R = 9.3 min (minor enantiomer) and peak 2, t_R = 8.9 min (major enantiomer).

3-Methyl-2,3-dihydrobenzofuran-4-carbaldehyde (22)
^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.06 (s, 1 H, CHO), 7.34–7.28 (m, 2 H, ArH × 2), 7.05–7.02 (m, 1 H, ArH), 4.60 [t, 1 H, J = 11.2 Hz, $CH_3CH(CH_2)OAr$], 4.34–4.29 [m, 1 H, one of $CH_3CH(CH_2)OAr$], 3.98–3.92 [m, 1 H, one of $CH_3CH(CH_2)OAr$], 1.30 (d, 3 H, J = 9.2 Hz, CH_3CH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.1, 160.6, 133.4, 132.7, 128.7, 124.8, 115.2, 79.3, 36.1, 20.5. HPLC analysis [AS column, hexanes–*i*-PrOH (99:1), 20 min run time]: peak 1, t_R = 10.0 min (minor enantiomer) and peak 2, t_R = 8.9 min (major enantiomer).

***tert*-Butyl-(3-isopropenyloxybenzylidene)amine (23)**
Imine **23** was prepared following the general procedure for imine formation. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.22 (s, 1 H, CH=NCH), 7.49 (d, 1 H, J = 7.6 Hz, ArH), 7.44 (s, 1 H, ArH), 7.34 (t, 1 H, J = 8.0 Hz, ArH), 7.06 (d, 1 H, J = 7.6 Hz, ArH), 4.17 [s, 1 H, one of CH_2=C(CH_3)OAr], 3.97 [s, 1 H, one of CH_2=C(CH_3)OAr], 1.98 (s, 3 H, CCH_3), 1.28 [s, 9 H, $C(CH_3)_3$]. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.4, 155.6, 154.4, 138.9, 129.5, 123.5, 122.5, 119.8, 89.9, 57.3, 29.6, 20.0. HRMS–FAB: *m/z* calcd for $C_{14}H_{20}NO$ $[M + H]^+$: 218.1545; found: 218.1545.

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